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ISOQUINOLINE DERIVATIVES HAVING KINASE INHIBITORY ACTIVITY
AND MEDICAMENT CONTAINING THE SAME
This application is a 371 of PCT/JP03/11733 filed 9/12/2003.

BACKGROUND OF THE INVENTION

5 Field of the Invention

The present invention relates to isoquinoline derivatives having Rho kinase inhibitory activity, more particularly useful for the treatment of diseases media.

Background Art

10 It has been revealed that Rho is activated upon the receipt of signals from various cell membrane receptors, and the activated Rho functions, through ROCK/Rho kinase and, further, actomyosin system, as a molecular switch of a wide variety of cellular phenomena such as smooth muscle contraction, cell movement, cell adhesion, change in 15 character of cells (formation of actin stressed fibers), control of cell division (sthenia of cytokinesis or activation of gene transcription), platelet aggregation, leukocyte aggregation, cell proliferation, sthenia of carcinogenesis and invasion of cancer and the like.

20 The contraction of smooth muscle is deeply involved in the pathology of hypertension, angina pectoris, vasospasm, for example, cardiovascular contraction and cerebrovascular contraction, asthma, peripheral circulatory disorder, threatened premature birth, glaucoma, constriction of visual field, pollakiuria, impotence and the like... Cell movement plays an important role in invasion/metastasis of cancer, 25 arteriosclerosis, retinopathy, immune response and the like. Cell adhesion is deeply involved in metastasis of cancer, inflammation, and autoimmune diseases. The change of cell morphology is deeply involved in cerebral dysfunction, osteoporosis, microbism and the like. Cell proliferation is deeply involved in cancer, arteriosclerosis and the like. 30 Thus, Rho is deeply involved in various diseases.

ROCK or ROCK I (Japanese Patent Laid-Open No. 135683/1997; and T. Ishizaki et al., EMBO J., Vol. 15, No. 8, pp 1885-1893 (1996)) and Rho kinase or ROCK II (Japanese Patent Laid-Open No. 113187/1998; and T. Matsui et al., EMBO J., Vol. 15, No. 9, pp 2208-2216 (1996)) were 35 reported as serine/threonine kinase which is activated upon the activation of Rho and were shown to be isozymes (O. Nakagawa et al.,